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To: Commissioner of Patents and Trademarks
Washington, D.C. 20231

Response to Examiner's Action mailed 09/12/94
Serial Number : 08/031,562
Examiner: Julie Krsek-Staples,Ph.D.
Supervisory Patent Examiner: Christine M. Nucker
Group 180

This is in response to the Examiner's action of the above date.

Under the Examiner's "Response to Applicant's Arguments", page 5:

The Examiner acknowledges that anti-Recognin antibodies are cytotoxic to cancer cells, and notes that the presence of these antibodies is quantitatively associated with greater survival in human cancer patients; then the Examiner states:

"The statistical significance of the survival studies (in humans) shows that there is a correlation between anti-recognin antibodies and survival. However, it is not clear whether the antibodies themselves are capable of treating or preventing cancer or whether other factors are involved." (addition in parentheses is the Applicant's). The Examiner correctly cites for example tumor mass and tumor-host relationship as

relevant 'other factors'.

In response, the applicant agrees that of course other factors are involved in cancer prevention and treatment. But it is not claimed by the applicant that Recognin vaccines are sufficient to overcome all other variables or factors in cancer prevention or treatment, any more than any prevention or treatment in medicine is ever properly so-claimed.

However, it is very relevant that actual survival in human cancer patients, the end-measure of the pressure of all 'other factors', is quantitatively related to the concentration of anti-Recognin antibody. This fact cannot be cited, to the applicant's knowledge, by any other currently available vaccine or antibody treatment. (Neither Cantrell's nor Rapp's issued patents, which are cited by the Examiner against the apllicant's application, provide human data of such end-measure effectiveness of the so-called vaccines which they have used in animals only.)

For another example of the involvement of other factors, on page 85 of the reference supplied by and used by the Examiner (Freda K. Stevenson, Int. J Clin Lab Res 22:84-89,1992), Stevenson points out the problems in using all tumor-associated antigens (TAAs) (other than the Recognins) as potential vaccines as follows:

"The TAAs are products of some normal cells and are often differentiation antigens; ----for passive antibody, --it is often acceptable to destroy some normal cells together with the target tumor cells---However, in an active immune response, such attack would be continuous and theoretically could lead to autoimmunity."

In the case of the Recognins, this particular 'other factor' is not a problem, since

the Recognins are not constituents of normal cells, are not available for extraction as antigens in normal cells, are not stained by anti-Recognin antibody in normal cells, and therefore normal cells are not at risk in either active or passive treatment with the Recognins or anti-Recognins.

Under Examiner's "New Grounds for Rejection", p.5:

The Examiner's rejection under 35 U.S.C. of Claims 1 and 2 as unpatentable due to obviousness is fallacious since it does not appear to recognize the more stringent criteria adopted by both the Examiner's references, Stevenson and Bystryn, and by the applicant, for the claim of a "vaccine" compared to that adopted by Cantrell or Rapp. Thus in both Cantrell and Rapp:

1) Being a "tumor associated antigen" is sufficient. Clearly not, since all tumor associated antigens which are not viral associated place normal healthy cells at risk (see Stevenson above) except in the case of the Recognins. For example, an anti-CEA vaccine would probably devastate all of the normal mucosal cells of the colon.

2) Being an "oncoprotein" is sufficient. Clearly not, since many or all oncoproteins are constituents of normal cells (they normally increase in brain in learning, in many organs during development and healing) except for certain point mutations or changes associated with cancer which may not be sufficient to change their epitope constitution and thus they will be at risk from cytotoxic antibody just like "tumor associated antigens" except in the case of Recognins.

3) Animal experiments are sufficient. Clearly not, since some human evidence is useful, and this is provided in the case of the Recognins.

4) Not having direct evidence of either increase in specific cellular (eg. T cell) or antibody response to their "vaccines" is sufficient. Clearly not, since otherwise the effects observed in animals by Cantrell and Rapp could be due to other than

immunological mechanisms, and therefore not be the effects of a true vaccine. In the case of the Recognins, this direct effect has been observed in both specific antibody response, both in vitro and in vivo in cancer patients, and in cellular response in animals to reaction at the site of the injection.

5) Not having direct evidence of killing or stasis of cancer cells by specific T cells or specific antibody is sufficient for Cantrell and Rapp. Clearly not, for the Recognins have the direct evidence of killing and stasis of cancer cells at very low concentrations (picograms per cancer cell).

6) There is no evidence for the natural immunity mechanism which will be strengthened in both Cantrell and Rapp. This natural mechanism became clear for the Recognins when it was demonstrated that:

i) The anti-Recognins increase with age, in normal healthy non-tumor individuals (humans) as the risk for cancer increase;

ii) The anti-Recognins increase with age more strikingly, and start earlier, in healthy members of cancer high-risk families;

iii) While the Recognins, present in tumor cells, have been shown by studies of thousands of cancer patients to be a) able to induce clinically effective immune responses in humans, the anti-Recognins are powerful static and cytotoxic agents against cancer cells, because they interact with Recognin b) antigen which is expressed on the tumor to be treated, where it can be seen by, and can interact with, the immune effector mechanisms, i.e. on the external surface of the tumor cells (these requirements are a paraphrase of those stated by Bystryn,Cancer and Metastasis Reviews 9:81-91, 1990, page 83).

The Examiner has, with respect, mistakenly assumed that just being a tumor-associated antigen or an oncoprotein is enough to make a vaccine, hence with just